

(19) World Intellectual Property
Organization
International Bureau



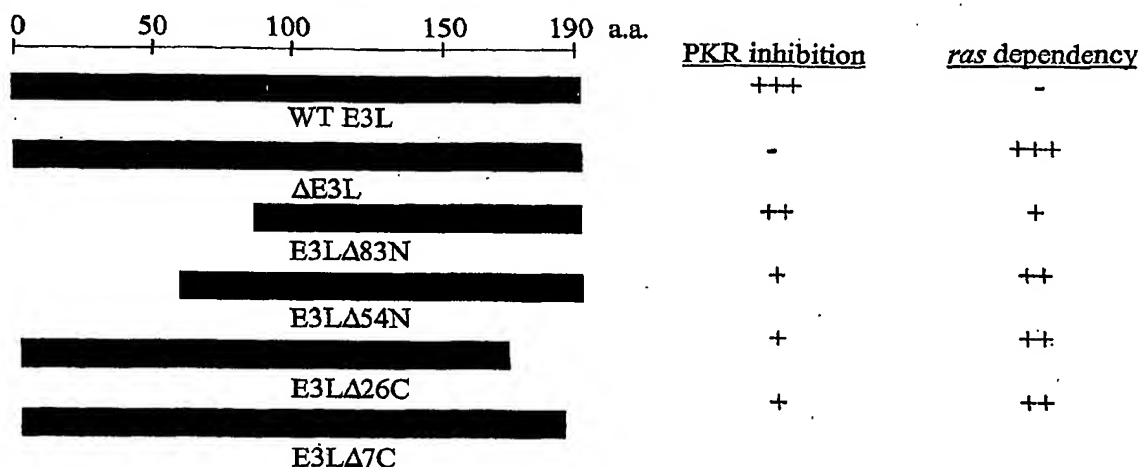
(43) International Publication Date
27 January 2005 (27.01.2005)

PCT

(10) International Publication Number
WO 2005/007824 A2

- (51) International Patent Classification⁷: **C12N**
- (21) International Application Number:
PCT/US2004/022165
- (22) International Filing Date: 8 July 2004 (08.07.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/485,503 8 July 2003 (08.07.2003) US
- (71) Applicant (for all designated States except US): **ARI-ZONA BOARD OF REGENTS [US/US];** P.O. Box 879209, Tempe, AZ 85287-9209 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **JACOBS, Bertram [US/US];** 1004 S. Wilson Street, Tempe, AZ 85281 (US). **MITNIK, Chandra [US/US];** 1056 E. Sandpiper Drive, Tempe, AZ 85283 (US). **LANGLAND, Jeffrey [US/US];** 506 W. El Alba Way, Chandler, AZ 85225 (US).
- (74) Agents: **BUTTER, Gary, M et al.;** Baker Botts LLP, 30 Rockefeller Plaza, New York, NY 10112-4498, NY 10112 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— without international search report and to be republished upon receipt of that report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **MUTANTS OF VACCINIA VIRUS AS ONCOLYTIC AGENTS**



(57) Abstract: The present invention relates to mutant oncolytic vaccinia viruses and their use for selective destruction of cancer cells. The mutant vaccinia viruses of the invention include those having a reduced ability to inhibit the antiviral dsR-NA dependent protein kinase (PKR) and increased sensitivity to interferon. Such mutants include, for example, vaccinia viruses having mutations in the E3L and/or K3L regions. The invention is based on the discovery that vaccinia viruses having mutations in the E3L region are capable of replication in oncogenic cells resulting in cell lysis. The invention further provides methods for treating proliferative disorders, such as neoplasms, in a host comprising administration of mutant vaccinia virus under conditions which result in substantial lysis of the proliferating cancer cells.